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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/918,715

08/01/2001

Brad St. Croix

001107.00134

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03/19/2004

BANNER & WITCOFF

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WASHINGTON, DC 20001

EXAMINER

YAEN, CHRISTOPHER H

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/918,715

Applicant(s)

ST. CROIX ET AL.

Examiner

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-37 is/are pending in the application.
- 4a) Of the above claim(s) 11-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 18-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

RE: St Croix *et al.*

Earliest Filing Date: 2 August 2000

1. The amendment filed 1/22/2004 is acknowledged and entered into the record. Accordingly, claims 18-37 are newly added.
2. Claims 1-10, and 18-37 are therefore pending and examined on the merits.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Information Disclosure Statement

4. The Information Disclosure Statements filed 4/23/2003, 5/02/2003, 5/8/2003, and 1/22/2004 are acknowledged and considered. A signed copy of the IDS is attached hereto.

Claim Rejections Maintained - 35 USC § 101 & 35 USC § 112, 1st paragraph

5. The rejection of claims 1-10 and now newly added claims 18-37 under 35 USC 101 and 35 USC 112, 1st paragraph as lacking a well established utility is maintained for the reasons of record. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

Applicant states that the disclosed utility of the claimed molecule includes inhibiting neoangiogenesis, inhibiting tumor growth, isolating endothelial cells, and use as a diagnostic tool, and that the claimed utilities are deemed appropriate to satisfy the

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requirements under 35 USC 101. It is also asserted that the biological function or mechanism of the protein to which the claimed molecule binds is not required under the law and that the use of the invention as a diagnostic and or therapeutic agent is considered a well-established utility with real world applicability. Applicant also responds to arguments concerning the regulation of protein translation arguing that the expression of mRNA levels correlate with protein levels. Finally, applicant argues that the use of SAGE analysis is viewed as a meaningful analysis of differential expression of protein and argues that others have already shown that TEM protein are engaged in ECM remodeling, cytoskeletal reorganization, and cell migration.

The specification discloses 46 genes that are differentially expressed in tumor endothelium. Specifically TEM 17 (SEQ ID No: 230) was shown to be one of the genes that tend to be expressed in tumor endothelial cells but absent in normal endothelial cells (see page 17). The specification further states the function of many of the TEM proteins are unknown and that those that have been previously characterized have been associated with ECM formation and remodeling (see page 26). Aside from the brief characterization provided on page 32 under "TEM 17" and its differential mRNA expression pattern in tumor endothelium (page 56), the specification offers little information about the actual existence of the TEM 17 protein or its functional role. Without this, the use of antibodies or fragments thereof would not be considered a substantial utility, and the artisan is essentially left with a starting point from which further investigation is to be performed. There is no record either in the prior art or in the specification of what the protein's function is, or its relation to a specific type of

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disease, and as such an antibody or fragments thereof which binds to the said protein has not been defined with a real world utility, because the binding of the antibody to an unknown protein in either a diagnostic or therapeutic manner does nothing but bind and as such is not considered a specific utility (i.e. ~~what would it do?~~). Moreover, no data with regard to its actual existence as a protein has been offered, and because the characterization of its structural features has only been done so by comparing with homologues, the utility claimed for its homologues cannot be applied to the TEM 17 protein to which the antibody and its fragments is to bind.

Although it is true that the biological function or mechanism of a protein is not required for there to be a patentable utility, there must be some indication that the protein is useful in some real world applicability. Therefore, claims to an antibody that bind to a protein which has not been established as having a substantial and or specific utility cannot possibly be useful for either therapy or in diagnostic applications because what would the artisan use an antibody to detect or treat? (see Utility Guidelines example 12)

Great!

Applicant's arguments concerning expression of mRNA levels as being indicative of protein expression is not found persuasive. The references cited and provided in the previous office action serve as examples of the disconnect between protein and mRNA expression levels and how the expression of one molecule cannot be correlated to another. As of the filing date, neither the art of recordⁿ or the specification has taught that the protein itself is actually translated. Therefore, if there is no proof that the protein has actually been translated, the use of an antibody for diagnostic or

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therapeutic value has not been clearly established because a differential expression of the protein would be required for use in either applications.

Finally, SAGE analysis is only indicative of differential mRNA expression and does not definitively indicate that proteins are expressed at levels similar to that found in the analysis. Further, ^{the teachings of} Novatchkova and Eisenhaber ^{findings do not} give any indication of the role of TEM17, and ^{provide mere speculation} ~~has~~ only ~~postulated~~ that the function of TEM family of proteins are in general useful in ECM remodeling, cytoskeletal reorganization, and cell migration, but has not commented on the role of TEM17 itself. The fact that TEM17 is a member of the family is not in question, but rather the utility or function that is associated with other member of TEM family cannot be applied to that of TEM17, and as such, utilities for those TEM proteins cannot also be applied to TEM17.

Therefore, the instant application has not set forth a well established, substantial or specific utility for the claimed invention and as such, the rejection under 35 USC 101 and 112, 1st paragraph is maintained.

Claim Rejections Maintained - 35 USC § 102

6. The rejection of claims 1 and 2 and now newly presented claims 32-33 under 35 USC 102 (b) is maintained for the reasons of record. Applicant argues that the prior art teach^{ing} of Jacobs *et al* would not have lead one of skill in the art to make an antibody that is identical to that instantly claimed, because the protein taught by Jacobs *et al* is different from that of SEQ ID No: 230. Applicant points to the fact that the sequence taught by Jacobs *et al* is only 108 amino acids long of which the first 100 amino acids

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are taught as being a leader/ signal sequence and therefore not present in the mature protein. Applicant also points out that the extracellular domain of TEM 17 extends to only amino acid 427 of SEQ ID No: 230. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. The claims are to be given its broadest reasonable interpretation. In this case Jacobs *et al* teach a sequence that is identical in part to SEQ ID No: 230 (i.e. 100 % homology exists between amino acid 383-450 of SEQ ID No: 230 and amino acid 41-108 of Jacobs *et al*). Because the sequence taught by Jacobs *et al* falls within the extracellular domain of SEQ ID No: 230, and because Jacobs *et al* disclose antibodies that can bind to sequences disclosed, the antibody as broadly claimed is anticipated by Jacobs *et al* regardless of whether Jacobs *et al* teaches away from a protein that is identical to that being claimed. The question whether a reference "teaches away" from the invention is inapplicable to an anticipation analysis. *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998) (The prior art was held to anticipate the claims even though it taught away from the claimed invention. "The fact that a modem with a single carrier data signal is shown to be less than optimal does not vitiate the fact that it is disclosed."). See also *Atlas Powder Co. v. IRECO, Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999) (Claimed composition was anticipated by prior art reference that inherently met claim limitation of "sufficient aeration" even though reference taught away from air entrapment or purposeful aeration.) – see MPEP 2131.05.

Therefore, the claims are still anticipated by Jacobs *et al* and the rejection is therefore maintained for the reasons of record.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 1/22/2004.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

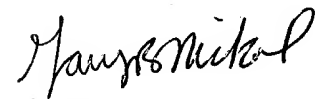
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
March 16, 2004



GARY NICKOL
PRIMARY EXAMINER